



## Donor 5411

### Genetic Testing Summary

Fairfax Cryobank recommends reviewing this genetic testing summary with your healthcare provider to determine suitability.

Last Updated: 03/20/20

Donor Reported Ancestry: Korean

Jewish Ancestry: No

| Genetic Test*   | Result  | Comments/Donor's Residual Risk**  |
|---|---|---|
| Chromosome analysis (karyotype)                           | Normal male karyotype                               | No evidence of clinically significant chromosome abnormalities  |
| Hemoglobin evaluation                                     | Normal hemoglobin fractionation and MCV/MCH results | Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies |
| Cystic Fibrosis (CF) carrier screening                    | Negative by gene sequencing in the CFTR gene        | 1/4796  |
| Spinal Muscular Atrophy (SMA) carrier screening           | Negative for deletions of exon 7 in the SMN1 gene   | 1/628   |
| Standard testing attached- 22 diseases by gene sequencing | Negative for genes sequenced                        |   |
| <b>Special Testing</b>                                    |   |   |
| Non-Syndromic Hearing Loss (GJB2)                         | Negative by gene sequencing in the GJB2 gene        | 1/280   |

\*No single test can screen for all genetic disorders. A negative screening result significantly reduces, but cannot eliminate, the risk for these conditions in a pregnancy.

\*\*Donor residual risk is the chance the donor is still a carrier after testing negative.

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**Ordering Practice:**

Practice Code: [REDACTED]  
Fairfax Cryobank: [REDACTED]  
[REDACTED]  
Physician: [REDACTED]  
Report Generated: 2016-12-29

**5411** [REDACTED]

DOB: [REDACTED]  
Gender: Male  
Ethnicity: East Asian  
Procedure ID: 77156  
Kit Barcode: [REDACTED]  
Specimen: Blood, #78000  
Specimen Collection: 2016-12-09  
Specimen Received: 2016-12-12  
Specimen Analyzed: 2016-12-29

**Partner Not Tested**

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**TEST INFORMATION**

Test: CarrierMap<sup>SEQ</sup> (Genotyping & Sequencing)  
Panel: Fairfax Cryobank Panel V2- Sequencing  
Diseases Tested: 22  
Genes Tested: 22  
Genes Sequenced: 18

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**SUMMARY OF RESULTS: NO MUTATIONS IDENTIFIED**

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5411 [REDACTED] was not identified to carry any pathogenic mutations in the gene(s) tested.

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No pathogenic mutations were identified in the genes tested, reducing but not eliminating the chance to be a carrier for the associated genetic diseases. CarrierMap assesses carrier status for genetic disease via molecular methods including targeted mutation analysis and/ or next-generation sequencing; other methodologies such as CBC and hemoglobin electrophoresis for hemoglobinopathies and enzyme analysis for Tay-Sachs disease may further refine risks for these conditions. Results should be interpreted in the context of clinical findings, family history, and/or other testing. A list of all the diseases and mutations screened for is included at the end of the report. This test does not screen for every possible genetic disease.

For additional disease information, please visit [recombine.com/diseases](http://recombine.com/diseases). To speak with a Genetic Counselor, call **855.OUR.GENES**.

Assay performed by   
**Reprogenetics**  
CLIA ID: 31D1054821  
3 Regent Street, Livingston, NJ 07039  
Lab Technician: Bo Chu

Recombine CLIA # 31D2100763  
Reviewed by Pere Colls, PhD, HCLD, Lab Director

## ADDITIONAL RESULTS: NO INCREASED REPRODUCTIVE RISK

The following results are not associated with an increased reproductive risk.

| Disease (Gene)                                | 5411 [REDACTED]   | Partner Not Tested |
|---|---|--------------------|
| Spinal Muscular Atrophy: SMN1 Linked (SMN1) * | SMN1 Copy Number: 2 or more copies<br>Method: dPCR & Genotyping |                    |

### \* SMA Risk Information for Individuals with No Family History of SMA

|                  | Detection Rate | Pre-Test Carrier Risk | Post-Test Carrier Risk (2 SMN1 copies) | Post-Test Carrier Risk (3 SMN1 copies) |
|------------------|----------------|-----------------------|--|--|
| European         | 95%            | 1/35                  | 1/632                                  | 1/3,500                                |
| Ashkenazi Jewish | 90%            | 1/41                  | 1/350                                  | 1/4,000                                |
| Asian            | 93%            | 1/53                  | 1/628                                  | 1/5,000                                |
| African American | 71%            | 1/66                  | 1/121                                  | 1/3,000                                |
| Hispanic         | 91%            | 1/117                 | 1/1,061                                | 1/11,000                               |

For other unspecified ethnicities, post-test carrier risk is assumed to be <1%. For individuals with multiple ethnicities, it is recommended to use the most conservative risk estimate.

## Methods and Limitations

**Genotyping:** Genotyping is performed using the Illumina Infinium Custom HD Genotyping assay to identify mutations in the genes tested. The assay is not validated for homozygous mutations, and it is possible that individuals affected with disease may not be accurately genotyped.

**Sequencing:** Sequencing is performed using a custom next-generation sequencing (NGS) platform. Only the described exons for each gene listed are sequenced. Variants outside of these regions may not be identified. Some splicing mutations may not be identified. Triplet repeat expansions, intronic mutations, and large insertions and deletions may not be detected. All identified variants are curated, and determination of the likelihood of their pathogenicity is made based on examining allele frequency, segregation studies, predicted effect, functional studies, case/control studies, and other analyses. All variants identified via sequencing that are reported to cause disease in the primary scientific literature will be reported. Variants considered to be benign and variants of unknown significance (VUS) are NOT reported.

**Spinal Muscular Atrophy:** Carrier status for SMA is assessed via copy number analysis by dPCR and via genotyping. Some individuals with a normal number of SMN1 copies (2 copies) may carry both copies of the gene on the same allele/chromosome; this analysis is not able to detect these individuals. Thus, a normal SMN1 result significantly reduces but does not eliminate the risk of being a carrier. Additionally, SMA may be caused by non-deletion mutations in the SMN1 gene; CarrierMap tests for some, but not all, of these mutations. Some SMA cases arise as the result of de novo mutation events which will not be detected by carrier testing.

**Limitations:** In some cases, genetic variations other than that which is being assayed may interfere with mutation detection, resulting in false-negative or false-positive results. Additional sources of error include, but are not limited to: sample contamination, sample mix-up, bone marrow transplantation, blood transfusions, and technical errors. The test does not test for all forms of genetic disease, birth defects, and intellectual disability. All results should be interpreted in the context of family history; additional evaluation may be indicated based on a history of these conditions. Additional testing may be necessary to determine mutation phase in individuals identified to carry more than one mutation in the same gene. All mutations included within the genes assayed may not be detected, and additional testing may be appropriate for some individuals.

This test was developed and its performance determined by Recombine, Inc., and it has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.

## Diseases & Mutations Assayed

**Alpha Thalassemia (HBA1, HBA2):** Mutations (9): ♂ Genotyping | SEA deletion, c.207C>A (p.N69K), c.223G>C (p.D75H), c.2T>C (p.M1T), c.207C>G (p.N69K), c.340\_351delCTCCCGCCGAG (p.L114\_E117del), c.377T>C (p.L126P), c.427T>C (p.X143Qext32), c.\*+94A>G

**Beta Thalassemia (HBB):** Mutations (81): ♂ Genotyping | c.124\_127delTTCT (p.F42Lfs), c.17\_18delCT, c.20delA (p.E7Gfs), c.217insA (p.S73Kfs), c.223+702\_444+342del620insAAGTAGA, c.230delC, c.25\_26delAA, c.315+1G>A, c.315+2T>C, c.316-197C>T, c.316-146T>G, c.315+745C>G, c.316-1G>A, c.316-1G>C, c.316-2A>G, c.316-3C>A, c.316-3C>G, c.4delG (p.V2Cfs), c.51delC (p.K18Rfs), c.93-21G>A, c.92+1G>A, c.92+5G>A, c.92+5G>C, c.92+5G>T, c.92+6T>C, c.93-1G>A, c.93-1G>T, c.-50A>C, c.-78a>g, c.-79a>g, c.-81a>g, c.52A>T (p.K18X), c.-137C>g, c.-138C>t, c.-151C>T, c.118C>T (p.Q40X), c.169G>C (p.G57R), c.295G>A (p.V99M), c.415G>C (p.A139P), c.47G>A (p.W16X), c.48G>A (p.W16X), c.-80T>a, c.2T>C (p.M1T), c.75T>A (p.G25G), c.444+111A>G, c.-29g>a, c.68\_74delAAGTTGG, c.92G>C (p.R31T), c.92+1G>T, c.93-15T>G, c.93-1G>C, c.112delT, c.113G>A (p.W38X), c.114G>A (p.W38X), c.126delC, c.444+113A>G, c.250delG, c.225delC, c.383\_385delAGG (p.Q128\_A129delQAlnsP), c.321\_322insG (p.N109fs), c.316-1G>T, c.316-2A>C, c.287\_288insA (p.L97fs), c.271G>T (p.E91X), c.203\_204delTG (p.V68Afs), c.154delC (p.P52fs), c.135delC (p.F46fs), c.92+2T>A, c.92+2T>C, c.90C>T (p.G30G), c.84\_85insC (p.L29fs), c.59A>G (p.N20S), c.46delT (p.W16Gfs), c.45\_46insG (p.L16fs), c.36delT (p.T13fs), c.2T>G (p.M1R), c.1A>G (p.M1V), c.-137C>t, c.-136C>g, c.-142C>t, c.-140C>t Sequencing | NM\_000518:1-3

**Bloom Syndrome (BLM):** Mutations (25): ♂ Genotyping | c.2207\_2212delATCTGAGinsTAGATTC (p.Y736Lfs), c.2407insT, c.557\_559delCAA (p.S186K), c.1284G>A (p.W428X), c.1701G>A (p.W567X), c.1933C>T (p.Q645X), c.2528C>T (p.T843I), c.2695C>T (p.R899X), c.3107G>T (p.C1036F), c.2923delC (p.Q975K), c.3558+1G>T, c.3875-2A>G, c.2074+2T>A, c.2343\_2344dupGA (p.781EfsX), c.318\_319insT (p.L107fs), c.380delC (p.127Tfs), c.3564delC (p.1188Dfs), c.4008delG (p.1336Rfs), c.947C>G (p.S316X), c.2193+1\_2193+9del9, c.1642C>T (p.Q548X), c.3143delA (p.1048NfsX), c.356\_357delTA (p.C120Hfs), c.4076+1delG, c.3281C>A (p.S1094X) Sequencing | NM\_000057:2-22

**Canavan Disease (ASPA):** Mutations (8): ♂ Genotyping | c.433-2A>G, c.854A>C (p.E285A), c.693C>A (p.Y231X), c.914C>A (p.A305E), c.71A>G (p.E24G), c.654C>A (p.C218X), c.2T>C (p.M1T), c.79G>A (p.G27R) Sequencing | NM\_000049:1-6

**Cystic Fibrosis (CFTR):** Mutations (150): ♂ Genotyping | c.1029delC, 1153\_1154insAT, c.1477delCA, c.1519\_1521delATC (p.507delI), c.1521\_1523delCTT (p.508delF), c.1545\_1546delTA (p.Y515Xfs), c.1585-1G>A, c.164+12T>C, c.1680-886A>G, c.1680-1G>A, c.1766+1G>A, c.1766+1G>T, c.1766+5G>T, c.1818del84, c.1911delG, c.1923delCTCAAACTinsA, c.1973delGAAATCAATCTinsAGAAA, c.2052delA (p.K684fs), c.2052insA (p.Q685fs), c.2051\_2052delAAinsG (p.K6845fsX38), c.2174insA, c.261delIT, c.2657+5G>A, c.273+1G>A, c.273+3A>C, c.274-1G>A, c.2988+1G>A, c.3039delC, c.3140-26A>G, c.325delTAAinsG, c.3527delC, c.3535delACCA, c.3691delT, c.3717+12191C>T, c.3744delA, c.3773\_3774insT (p.L1258fs), c.442delA, c.489+1G>T, c.531delT, c.579+1G>T, c.579+5G>A (IVS4+5G>A), c.803delA (p.N268fs), c.805\_806delAT (p.1269fs), c.933\_935delCTT (p.311delF), c.946delT, c.1645A>C (p.S549R), c.2128A>T (p.K710X), c.1000C>T (p.R334W), c.1013C>T (p.T338I), c.1364C>A (p.A455E), c.1477C>T (p.Q493X), c.1572C>A (p.C524X), c.1654C>T (p.Q552X), c.1657C>T (p.R553X), c.1721C>A (p.P574H), c.2125C>T (p.R709X), c.223C>T (p.R75X), c.2668C>T (p.Q890X), c.3196C>T (p.R1066C), c.3276C>G (p.Y1092X), c.3472C>T (p.R1158X), c.3484C>T (p.R1162X), c.349C>T (p.R117C), c.3587C>G (p.S1196X), c.3712C>T (p.Q1238X), c.3764C>A (p.S1255X), c.3909C>G (p.N1303K), c.1040G>A (p.R347H), c.1040G>C (p.R347P), c.1438G>T (p.G480C), c.1558G>T (p.V520F), c.1624G>A (p.G542X), c.1646G>G (p.S549R), c.1646G>T (p.S549I), c.1652G>A (p.G551D), c.1675G>A (p.A559T), c.1679G>C (p.R560T), c.178G>T (p.E60X), c.1865G>A (p.G622D), c.254G>A (p.G85E), c.271G>A (p.G91R), c.274G>T (p.E92X), c.3209G>A (p.R1070Q), c.3266G>A (p.W1089X), c.3454G>C (p.D1152H), c.350G>A (p.R117H), c.3611G>A (p.W1204X), c.3752G>A (p.S1251N), c.3846G>A (p.W1282X), c.3848G>T (p.R1283M), c.532G>A (p.G178R), c.988G>T (p.G330X), c.1090T>C (p.S364P), c.3302T>A (p.M1101K), c.617T>G (p.L206W), c.14C>T (p.P51), c.19G>T (p.E7X), c.171G>A (p.W57X), c.313delA (p.I105fs), c.328G>C (p.D110H), c.580-1G>T, c.1055G>A (p.R352Q), c.1075C>A (p.Q359F), c.1079C>A (p.T360K), c.1647T>G (p.S549R), c.1976delA (p.N659fs), c.2290C>T (p.R764X), c.2737\_2738insG (p.Y913X), c.3067\_3072delATAGTG (p.I1023\_V1024delT), c.3536\_3539delCCAA (p.T1179fs), c.3659delC (p.T1220fs), c.54-5940\_273+10250del21080bp (p.S18fs), c.4364C>G (p.S1455X), c.4003C>T (p.L1335F), c.2538G>A (p.W846X), c.200C>T (p.P67L), c.4426C>T (p.Q1476X), c.1116+1G>A, c.1986\_1989delAACT (p.T663R), c.2089\_2090insA (p.R697Kfs), c.2215delG (p.V739Y), c.2637>G (p.L196X), c.3022delG (p.V1008S), c.3908dupA (p.N1303Kfs), c.658C>T (p.Q220X), c.868C>T (p.Q290X), c.1526delG (p.G509fs), c.2908+1085-3367+260del7201, c.11C>A (p.S4X), c.3878\_3881delTAA (p.V1293fs), c.3700A>G (p.I1234V), c.416A>T (p.H139L), c.366T>A (p.Y122X), c.3767\_3768insC (p.A1256fs), c.613C>T (p.P205S), c.293A>G (p.Q98R), c.3731G>A (p.G1244E), c.535C>A (p.Q179K), c.3368-2A>G, c.455T>G (p.M152R), c.1610\_1611delC (p.D537fs), c.3254A>G (p.H1085R), c.496A>G (p.K166E), c.1408\_1417delGTGATTATG (p.V470fs), c.1585-8G>A, c.2909G>G (p.G970D), c.653T>A (p.L218X), c.1175T>G (p.V392G), c.3139\_3139+1delGG, c.3717+4A>G (IVS22+4A>G) Sequencing | NM\_000492:1-27

**Familial Dysautonomia (IKBKAP):** Mutations (4): ♂ Genotyping | c.2204+6T>C, c.2741C>T (p.P914L), c.2087G>C (p.R696P), c.2128C>T (p.Q710X) Sequencing | NM\_003640:2-37

**Familial Hyperinsulinism: Type 1: ABCC8 Related (ABCC8):** Mutations (11): ♂ Genotyping | c.3989-9G>A, c.4159\_4161delITC (p.1387delF), c.4258C>T (p.R1420C), c.4477C>T (p.R1493W), c.2147G>T (p.G716V), c.4055G>C (p.R1352P), c.560T>A (p.V187D), c.4516G>A (p.E1506K), c.2506C>T (p.Q836X), c.579+2T>A, c.1333-1013A>G (IVS8-1013A>G) Sequencing | NM\_000352:1-39

**Fanconi Anemia: Type C (FANCC):** Mutations (8): ♂ Genotyping | c.456+4A>T, c.67delG, c.37C>T (p.Q13X), c.553C>T (p.R185X), c.1661T>C (p.L554P), c.1642C>T (p.R548X), c.66G>A (p.W22X), c.65G>A (p.W22X) Sequencing | NM\_000136:2-15

**Gaucher Disease (GBA):** Mutations (6): ♂ Genotyping | c.84\_85insG, c.1226A>G (p.N409S), c.1343A>T (p.D448V), c.1504C>T (p.R502C), c.1297G>T (p.V433L), c.1604G>A (p.R535H)

**Glycogen Storage Disease: Type IA (G6PC):** Mutations (13): ♂ Genotyping | c.376\_377insTA, c.79delC, c.979\_981delITC (p.327delF), c.1039C>T (p.Q347X), c.247C>T (p.R83C), c.724C>T (p.Q242X), c.248G>A (p.R83H), c.562G>C (p.G188R), c.648G>T, c.809G>T (p.G270V), c.113A>T (p.D38V), c.975delG (p.L326fs), c.724delC Sequencing | NM\_000151:1-5

**Joubert Syndrome (TMEM216):** Mutations (2): ♂ Genotyping | c.218G>T (p.R73L), c.218G>A (p.R73H) Sequencing | NM\_001173991:1-5

**Maple Syrup Urine Disease: Type 1B (BCKDHB):** Mutations (6): ♂ Genotyping | c.1114G>T (p.E372X), c.548G>C (p.R183P), c.832G>A (p.G278S), c.970C>T (p.R324X), c.487G>T (p.E163X), c.853C>T (p.R285X) Sequencing | NM\_183050:1-10

**Maple Syrup Urine Disease: Type 3 (DLD):** Mutations (8): ♂ Genotyping | c.104\_105insA, c.685G>T (p.G229C), c.214A>G (p.K72E), c.1081A>G (p.M361V), c.1123G>A (p.E375K), c.1178T>C (p.I393T), c.1463C>T (p.P488L), c.1483A>G (p.R495G) Sequencing | NM\_000108:1-14

**Mucopolidosis: Type IV (MCOLN1):** Mutations (5): ♂ Genotyping | c.-1015\_788del6433, c.406-2A>G, c.1084G>T (p.D362Y), c.304C>T (p.R102X), c.244delC (p.L82fsX) Sequencing | NM\_020533:1-14

**Nemaline Myopathy: NEB Related (NEB):** Mutations (2): ♂ Genotyping | c.7434\_7536del2502bp, c.8890-2A>G (IVS63-2A>G) Sequencing | NM\_001164508:63-66,86,95-96,103,105,143,168-172, NM\_000454:3-149

**Niemann-Pick Disease: Type A (SMPD1):** Mutations (6): ♂ Genotyping | c.996delC, c.1493G>T (p.R498L), c.911T>C (p.L304P), c.1267C>T (p.H423Y), c.1734G>C (p.K578N), c.1493G>A (p.R498H) Sequencing | NM\_000543:1-6

**Sickle-Cell Anemia (HBB):** Mutations (1): ♂ Genotyping | c.20A>T (p.E7V) Sequencing | NM\_000518:1-3

**Spinal Muscular Atrophy: SMN1 Linked (SMN1):** Mutations (19): ♂ Genotyping | DEL EXON 7, c.22\_23insA, c.43C>T (p.Q15X), c.91\_92insT, c.305G>A (p.W102X), c.400G>A (p.E134K), c.439\_443delGAAAGT, c.558delA, c.585\_586insT, c.683T>A (p.L228X), c.734C>T (p.P245L), c.768\_778dupTGCTGATGCTT, c.815A>G (p.Y272C), c.821C>T (p.T274I), c.823G>A (p.G275S), c.834+2T>G, c.835-18\_835-12delCCTTTAT, c.835G>T, c.836G>T dPCR | DEL EXON 7

**Tay-Sachs Disease (HEXA):** Mutations (78): ♂ Genotyping | c.1073+1G>A, c.1277\_1278insATC, c.1421+1G>C, c.805+1G>A, c.532C>T (p.R178C), c.533G>A (p.R178H), c.805G>A (p.G269S), c.1510C>T (p.R504C), c.1496G>A (p.R499H), c.509G>A (p.R170Q), c.1003A>T (p.Q335F), c.910\_912delITC (p.305delF), c.749G>A (p.G250D), c.632T>C (p.F211S), c.629C>T (p.S210F), c.613delC, c.611A>G (p.H204R), c.598G>A (p.V200M), c.590A>C (p.K197T), c.571-1G>T, c.540C>G (p.Y180X), c.538T>C (p.Y180H), c.533G>T (p.R178L), c.508C>T (p.R170W), c.409C>T (p.R137X), c.380T>G (p.L127R), c.346+1G>C, c.116T>G (p.I339R), c.78G>A (p.W26X), c.1A>G (p.M1V), c.1495C>T (p.R499C), c.459+5G>A (IVS4+5G>A), c.1422-2A>G, c.535C>T (p.H179Y), c.1141delG (p.V381fs), c.796T>G (p.W266G), c.155C>A (p.S52X), c.426delT (p.F142fs), c.413-2A>G, c.570+3A>G, c.536A>G (p.H179R), c.1146+1G>A, c.736G>A (p.A246T), c.1302C>G (p.F434L), c.778C>T (p.P260S), c.1008G>T (p.I336H), c.1385A>T (p.E462V), c.964G>A (p.G322N), c.340G>A (p.E114K), c.1432G>A (p.G478R), c.1178G>C (p.R393P), c.805+1G>C, c.1426A>T (p.R476X), c.623A>T (p.D208V), c.1537C>T (p.Q513X), c.1511G>T (p.R504L), c.1307\_1308delTA (p.L436fs), c.571-8A>G, c.624\_627delTCTC (p.D208fs), c.1211\_1212delTG (p.L404fs), c.621T>G (p.D207E), c.1511G>A (p.R504H), c.1177C>T (p.R393X), c.2T>C (p.M1T), c.1292G>A (p.W431X), c.947\_948insA (p.Y316fs), c.607T>G (p.W203G), c.1061\_1063delITC (p.F354\_Y355delinsX), c.615delG (p.L205fs), c.805+2T>C, c.1123delG (p.E375fs), c.1121A>G (p.Q374R), c.1043\_1046delTCAA (p.F348fs), c.1510delC (p.R504fs), c.1451T>C (p.L484P), c.964G>T (p.R322Y), c.1351C>G (p.L451V), c.571-2A>G (IVS5-2A>G) Sequencing | NM\_000520:1-14

**Usher Syndrome: Type 1F (PCDH15):** Mutations (7): ♂ Genotyping | c.733C>T (p.R245X), c.2067C>A (p.Y684X), c.7C>T (p.R3X), c.1942C>T (p.R648X), c.1101delT (p.A367fsX), c.2800C>T (p.R934X), c.4272delA (p.L1425fs) Sequencing | NM\_001142763:2-35

**Usher Syndrome: Type 3 (CLRN1):** Mutations (5): ♂ Genotyping | c.144T>G (p.N48K), c.131T>A (p.M120K), c.567T>G (p.Y189X), c.634C>T (p.Q212X), c.221T>C (p.L74P) Sequencing | NM\_001195794:1-4

**Walker-Warburg Syndrome (FKTN):** Mutations (4): ♂ Genotyping | c.1167insA (p.F390fs), c.139C>T (p.R47X), c.748T>G (p.C250G), c.515A>G (p.H172R) Sequencing | NM\_006731:2-10

## Residual Risk Information

Detection rates are calculated from the primary literature and may not be available for all ethnic populations. The values listed below are for genotyping. Sequencing provides higher detection rates and lower residual risks for each disease. More precise values for sequencing may become available in the future.

| Disease   | Carrier Rate               | Detection Rate | Residual Risk |
|---|----------------------------|----------------|---------------|
| Alpha Thalassemia                               | ♂ General: 1/48            | 50.67%         | 1/97          |
| Beta Thalassemia                                | ♂ African American: 1/75   | 84.21%         | 1/475         |
|   | ♂ Indian: 1/24             | 74.12%         | 1/93          |
|   | ♂ Sardinians: 1/23         | 97.14%         | 1/804         |
|   | ♂ Spaniard: 1/51           | 93.10%         | 1/739         |
| Bloom Syndrome                                  | ♂ Ashkenazi Jewish: 1/134  | 96.67%         | 1/4,020       |
|   | ♂ European: Unknown        | 66.22%         | Unknown       |
|   | ♂ Japanese: Unknown        | 50.00%         | Unknown       |
| Canavan Disease                                 | ♂ Ashkenazi Jewish: 1/55   | 98.86%         | 1/4,840       |
|   | ♂ European: Unknown        | 53.23%         | Unknown       |
| Cystic Fibrosis                                 | ♂ African American: 1/62   | 69.99%         | 1/207         |
|   | ♂ Ashkenazi Jewish: 1/23   | 96.81%         | 1/721         |
|   | ♂ Asian: 1/94              | 65.81%         | 1/275         |
|   | ♂ European: 1/25           | 94.96%         | 1/496         |
|   | ♂ Hispanic American: 1/48  | 77.32%         | 1/212         |
|   | ♂ Native American: 1/53    | 84.34%         | 1/338         |
| Familial Dysautonomia                           | ♂ Ashkenazi Jewish: 1/31   | >99%           | <1/3,100      |
| Familial Hyperinsulinism: Type 1: ABCC8 Related | ♂ Ashkenazi Jewish: 1/52   | 98.75%         | 1/4,160       |
|   | ♂ Finnish: 1/101           | 45.16%         | 1/184         |
| Fanconi Anemia: Type C                          | ♂ Ashkenazi Jewish: 1/101  | >99%           | <1/10,100     |
|   | ♂ General: Unknown         | 30.00%         | Unknown       |
| Gaucher Disease                                 | ♂ Ashkenazi Jewish: 1/15   | 87.16%         | 1/117         |
|   | ♂ General: 1/112           | 31.60%         | 1/164         |
|   | ♂ Spaniard: Unknown        | 44.29%         | Unknown       |
|   | ♂ Turkish: 1/236           | 59.38%         | 1/581         |
| Glycogen Storage Disease: Type IA               | ♂ Ashkenazi Jewish: 1/71   | >99%           | <1/7,100      |
|   | ♂ Chinese: 1/159           | 80.00%         | 1/795         |
|   | ♂ European: 1/177          | 76.88%         | 1/765         |
|   | ♂ Hispanic American: 1/177 | 27.78%         | 1/245         |
|   | ♂ Japanese: 1/177          | 89.22%         | 1/1,641       |
| Joubert Syndrome                                | ♂ Ashkenazi Jewish: 1/92   | >99%           | <1/9,200      |
| Maple Syrup Urine Disease: Type 1B              | ♂ Ashkenazi Jewish: 1/97   | >99%           | <1/9,700      |
| Maple Syrup Urine Disease: Type 3               | ♂ Ashkenazi Jewish: 1/94   | >99%           | <1/9,400      |
|   | ♂ General: Unknown         | 68.75%         | Unknown       |
| Mucopolipidosis: Type IV                        | ♂ Ashkenazi Jewish: 1/97   | 96.15%         | 1/2,522       |
| Nemaline Myopathy: NEB Related                  | ♂ Ashkenazi Jewish: 1/108  | >99%           | <1/10,800     |

| Disease                      | Carrier Rate              | Detection Rate | Residual Risk |
|------------------------------|---------------------------|----------------|---------------|
| Niemann-Pick Disease: Type A | ♂ Ashkenazi Jewish: 1/101 | 95.00%         | 1/2,020       |
| Sickle-Cell Anemia           | ♂ African American: 1/10  | >99%           | <1/1,000      |
|                              | ♂ Hispanic American: 1/95 | >99%           | <1/9,500      |
| Tay-Sachs Disease            | ♂ Argentinian: 1/280      | 82.35%         | 1/1,587       |
|                              | ♂ Ashkenazi Jewish: 1/29  | 99.53%         | 1/6,177       |
|                              | ♂ Cajun: 1/30             | >99%           | <1/3,000      |
|                              | ♂ European: 1/280         | 25.35%         | 1/375         |
|                              | ♂ General: 1/280          | 32.09%         | 1/412         |
|                              | ♂ Indian: Unknown         | 85.71%         | Unknown       |
|                              | ♂ Iraqi Jewish: 1/140     | 56.25%         | 1/320         |
|                              | ♂ Japanese: 1/127         | 82.81%         | 1/739         |
|                              | ♂ Moroccan Jewish: 1/110  | 22.22%         | 1/141         |
|                              | ♂ Portuguese: 1/280       | 92.31%         | 1/3,640       |
|                              | ♂ Spaniard: 1/280         | 67.65%         | 1/865         |
|                              | ♂ United Kingdom: 1/161   | 71.43%         | 1/564         |
| Usher Syndrome: Type 1F      | ♂ Ashkenazi Jewish: 1/126 | 93.75%         | 1/2,016       |
| Usher Syndrome: Type 3       | ♂ Ashkenazi Jewish: 1/120 | >99%           | <1/12,000     |
|                              | ♂ Finnish: 1/134          | >99%           | <1/13,400     |
| Walker-Warburg Syndrome      | ♂ Ashkenazi Jewish: 1/150 | >99%           | <1/15,000     |

**Patient Information**

Name: Donor 5411  
 Date of Birth: [REDACTED]  
 Sema4 ID: [REDACTED]  
 Client ID: [REDACTED]  
 Indication: Carrier Testing

**Specimen Information**

Specimen Type: Purified DNA  
 Date Collected: 02/26/2020  
 Date Received: 02/28/2020  
 Final Report: 03/13/2020

**Referring Provider**

[REDACTED]  
 Fairfax Cryobank, Inc.  
 [REDACTED]  
 [REDACTED]

## Custom Carrier Screen (ECS)

Number of genes tested: 1

### SUMMARY OF RESULTS AND RECOMMENDATIONS

**Negative**

**Negative for all genes tested: *GJB2***

To view a full list of genes and diseases tested  
 please see Table 1 in this report

*AR=Autosomal recessive; XL=X-linked*

**Recommendations**

- Consideration of residual risk by ethnicity after a negative carrier screen is recommended for the other diseases on the panel, especially in the case of a positive family history for a specific disorder.

## Test description

This patient was tested for the genes listed above using one or more of the following methodologies: target capture and short-read sequencing, long-range PCR followed by short-read sequencing, targeted genotyping, and/or copy number analysis. Please note that negative results reduce but do not eliminate the possibility that this individual is a carrier for one or more of the disorders tested. Please view the Table of Residual Risks Based on Ethnicity at the end of this report or at [go.sema4.com/residualrisk](http://go.sema4.com/residualrisk) for gene transcripts, sequencing exceptions, specific detection rates, and residual risk estimates after a negative screening result. With individuals of mixed ethnicity, it is recommended to use the highest residual risk estimate. Only known pathogenic or likely pathogenic variants are reported. This carrier screening test does not report likely benign variants and variants of uncertain significance (VUS). If reporting of likely benign variants and VUS are desired in this patient, please contact the laboratory at 800-298-6470, option 2 to request an amended report.

**Rebekah Zimmerman, Ph.D., FACMG, Laboratory Director**

Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D.

## Genes and diseases tested

For specific detection rates and residual risk by ethnicity, please visit [go.sema4.com/residualrisk](https://go.sema4.com/residualrisk)

**Table 1: List of genes and diseases tested with detailed results**

| Disease  | Gene        | Inheritance Pattern | Status                            | Detailed Summary |
|--|-------------|---------------------|-----------------------------------|------------------|
| ⊖ Negative   |             |                     |                                   |                  |
| Non-Syndromic Hearing Loss ( <i>GJB2</i> -Related) | <i>GJB2</i> | AR                  | Reduced Risk<br>(see table below) |                  |

AR=Autosomal recessive; XL=X-linked

**Table 2: Residual Risk by ethnicity for negative results**

| Disease (Inheritance)  | Gene          | Ethnicity              | Carrier Frequency | Detection Rate | Residual Risk | Analytical Detection Rate |
|--|---------------|------------------------|-------------------|----------------|---------------|---------------------------|
| Non-Syndromic Hearing Loss ( <i>GJB2</i> -Related) (AR)<br>NM_004004.5 | <i>GJB2</i> † | African                | 1 in 56           | 85%            | 1 in 360      | 99%                       |
|  |               | Ashkenazi Jewish       | 1 in 13           | 94%            | 1 in 210      |                           |
|  |               | East Asian             | 1 in 5            | 98%            | 1 in 280      |                           |
|  |               | Finnish                | 1 in 16           | 99%            | 1 in 1,400    |                           |
|  |               | European (Non-Finnish) | 1 in 18           | 97%            | 1 in 600      |                           |
|  |               | Native American        | 1 in 28           | 96%            | 1 in 610      |                           |
|  |               | South Asian            | 1 in 55           | 94%            | 1 in 970      |                           |
|  |               | Worldwide              | 1 in 18           | 97%            | 1 in 530      |                           |

\* Carrier detection by HEXA enzyme analysis has a detection rate of approximately 98% (Applies to *HEXA* gene testing only).

† Carrier frequencies include milder and reduced penetrance forms of the disease. Therefore, carrier frequencies may appear higher than reported in the literature (Applies to *BTD*, *Fg*, *GJB2*, *GJB1*, *GLA*, and *MEFV* gene testing only).

‡ Please note that *GJB2* testing includes testing for the two upstream deletions, del(*GJB6*-D13S1830) and del(*GJB6*-D13S1854) (PMID:11807148 and 15994881) (Applies to *GJB2* gene testing only).

AR: Autosomal recessive; N/A: Not available; XL: X-linked

## Test methods and comments

Genomic DNA isolated from this patient was analyzed by one or more of the following methodologies, as applicable:

### Next Generation Sequencing (NGS) (Analytical Detection Rate >95%)

NGS was performed on a panel of genes for the purpose of identifying pathogenic or likely pathogenic variants.

Agilent SureSelect™QXT technology was used with a custom capture library to target the exonic regions and intron/exon splice junctions of the relevant genes, as well as a number of UTR, intronic or promoter regions that contain previously reported mutations. Samples were pooled and sequenced on the Illumina HiSeq 2500 platform in the Rapid Run mode or the Illumina NovaSeq platform in the Xp workflow, using 100 bp paired-end reads. The sequencing data was analyzed using a custom bioinformatics algorithm designed and validated in house. The coding exons and splice junctions of the known protein-coding RefSeq genes were assessed for the average depth of coverage (minimum of 20X) and data quality threshold values. Most exons not meeting a minimum of >20X read depth across the exon are further analyzed by Sanger sequencing. Please note that several genomic regions present difficulties in mapping or obtaining read depth >20X. The exons contained within these regions are noted within Table 1 (as "Exceptions") and will not be reflexed to Sanger sequencing if the mapping quality or coverage is poor. Any variants identified during testing in these regions are confirmed by a second method and reported if determined to be pathogenic or likely pathogenic. However, as there is a possibility of false negative results within these regions, detection rates and residual risks for these genes have been calculated with the presumption that variants in these exons will not be detected, unless included in the MassARRAY® genotyping platform.



This test will detect variants within the exons and the intron-exon boundaries of the target regions. Variants outside these regions may not be detected, including, but not limited to, UTRs, promoters, and deep intronic areas, or regions that fall into the Exceptions mentioned above. This technology may not detect all small insertion/deletions and is not diagnostic for repeat expansions and structural genomic variation. In addition, a mutation(s) in a gene not included on the panel could be present in this patient.

Variant interpretation and classification was performed based on the American College of Medical Genetics Standards and Guidelines for the Interpretation of Sequence Variants (Richards et al, 2015). All potentially pathogenic variants may be confirmed by either a specific genotyping assay or Sanger sequencing, if indicated. Any benign variants, likely benign variants or variants of uncertain significance identified during this analysis will not be reported.

#### Copy Number Variant Analysis (Analytical Detection Rate >95%)

Large duplications and deletions were called from the relative read depths on an exon-by-exon basis using a custom exome hidden Markov model (XHMM) algorithm. Deletions or duplications determined to be pathogenic or likely pathogenic were confirmed by either a custom arrayCGH platform, quantitative PCR, or MLPA (depending on CNV size and gene content). While this algorithm is designed to pick up deletions and duplications of 2 or more exons in length, potentially pathogenic single-exon CNVs will be confirmed and reported, if detected.

#### Exon Array (Confirmation method) (Accuracy >99%)

The customized oligonucleotide microarray (Oxford Gene Technology) is a highly-targeted exon-focused array capable of detecting medically relevant microdeletions and microduplications at a much higher resolution than traditional aCGH methods. Each array matrix has approximately 180,000 60-mer oligonucleotide probes that cover the entire genome. This platform is designed based on human genome NCBI Build 37 (hg19) and the CGH probes are enriched to target the exonic regions of the genes in this panel.

#### Quantitative PCR (Confirmation method) (Accuracy >99%)

The relative quantification PCR is utilized on a Roche Universal Library Probe (UPL) system, which relates the PCR signal of the target region in one group to another. To test for genomic imbalances, both sample DNA and reference DNA is amplified with primer/probe sets that specific to the target region and a control region with known genomic copy number. Relative genomic copy numbers are calculated based on the standard  $\Delta\Delta C_t$  formula.

#### Long-Range PCR (Analytical Detection Rate >99%)

Long-range PCR was performed to generate locus-specific amplicons for *CYP21A2*, *HBA1* and *HBA2* and *GBA*. The PCR products were then prepared for short-read NGS sequencing and sequenced. Sequenced reads were mapped back to the original genomic locus and run through the bioinformatics pipeline. If indicated, copy number from MLPA was correlated with the sequencing output to analyze the results. For *CYP21A2*, a certain percentage of healthy individuals carry a duplication of the *CYP21A2* gene, which has no clinical consequences. In cases where two copies of a gene are located on the same chromosome in tandem, only the second copy will be amplified and assessed for potentially pathogenic variants, due to size limitations of the PCR reaction. However, because these alleles contain at least two copies of the *CYP21A2* gene in tandem, it is expected that this patient has at least one functional gene in the tandem allele and this patient is therefore less likely to be a carrier. When an individual carries both a duplication allele and a pathogenic variant, or multiple pathogenic variants, the current analysis may not be able to determine the phase (cis/trans configuration) of the *CYP21A2* alleles identified. Family studies may be required in certain scenarios where phasing is required to determine the carrier status.

#### Residual Risk Calculations

Carrier frequencies and detection rates for each ethnicity were calculated through the combination of internal curations of >28,000 variants and genomic frequency data from >138,000 individuals across seven ethnic groups in the gnomAD database. Additional variants in HGMD and novel deleterious variants were also incorporated into the calculation. Residual risk values are calculated using a Bayesian analysis combining the *a priori* risk of being a pathogenic mutation carrier (carrier frequency) and the detection rate. They are provided only as a guide for assessing approximate risk given a negative result, and values will vary based on the exact ethnic background of an individual. This report does not represent medical advice but should be interpreted by a genetic counselor, medical geneticist or physician skilled in genetic result interpretation and the relevant medical literature.

#### Sanger Sequencing (Confirmation method) (Accuracy >99%)

Sanger sequencing, as indicated, was performed using BigDye Terminator chemistry with the ABI 3730 DNA analyzer with target specific amplicons. It also may be used to supplement specific guaranteed target regions that fail NGS sequencing due to poor quality or low depth of coverage (<20 reads) or as a confirmatory method for NGS positive results. False negative results may occur if rare variants interfere with amplification or annealing.

#### SELECTED REFERENCES

##### Carrier Screening

Grody W et al. ACMG position statement on prenatal/preconception expanded carrier screening. *Genet Med*. 2013 15:482-3.

##### Variant Classification:



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Richards S et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015 May;17(5):405-24  
Additional disease-specific references available upon request.